

validez, sensibilidad y especificidad^{2,11}. Habiendo cumplido con las expectativas del primer año de monitoreo, además de la implementación de programas de mejora, lo que sigue es ampliar el número de indicadores y ajustar los estándares con la nueva evidencia disponible. La expansión del monitoreo de calidad solo puede redundar en beneficios sin requerir grandes inversiones ni tecnología compleja.

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H1N1 influenza virus-associated encephalitis: A case report

Encefalitis asociada al virus de la gripe H1N1: un caso clínico

Febrile respiratory symptoms represent the most common clinical manifestations of infection with 2009 H1N1 virus and are in general mild and self-limited. Since the 2009 H1N1 pandemic several neurologic complications have been described. Children and young adults are preferentially affected. We report a case of H1N1-associated encephalitis in an adult patient.

A 56-year-old male nurse, with a past medical history significant for hypertension and right-sided nephrectomy for congenital hydronephrosis, was admitted, initially to the emergency department of another hospital, with a 5-day history of influenza-like illness including lethargy, high fever and nonproductive cough. A nasopharyngeal swab was performed to test for the H1N1 virus.

On admission the patient was febrile, but otherwise his other vital signs were stable. He was conscious and oriented. The rest of the physical and neurologic examination was unremarkable.

Laboratory studies revealed normal white blood cell count, thrombocytopenia of $77 \times 10^9/L$ and elevated C-reactive protein of 15.8 mg/dL. Serum electrolytes and renal

and liver function tests were within normal limits. Chest radiograph demonstrated consolidation of the left lower lobe. He was diagnosed with community-acquired pneumonia and broad-spectrum antibiotic therapy consisted of intravenous ceftriaxone and azithromycin was initiated. On day 2 of hospitalization antiviral therapy with Oseltamivir 150 mg/day was associated after nasopharyngeal swab confirmed H1N1 virus infection.

Despite antibiotic and antiviral therapies, his respiratory status worsened. On day 3 he developed acute respiratory distress syndrome requiring intubation and he was transferred to the intensive care unit.

Therapy with Oseltamivir was discontinued after 9 days. Throughout his ICU-stay he remained febrile. After successful weaning from mechanical ventilation and sedation the patient was extubated on ICU-day 10. During the following day's he was noted to have fever, fluctuating mental status and disorientation.

A computed tomography scan of the brain showed bilateral cortical and subcortical vasogenic cerebral edema with areas of hemorrhage, involving the right frontoparietal lobe, the left occipital lobe and the left cerebellar hemisphere, with mass effect on the left ventricle with midline shift and subfalcine and right-sided uncal herniation.

The patient was put on antiedemic therapy and transferred to our institution for observation by neurosurgery. Just before being transported he required reintubation for

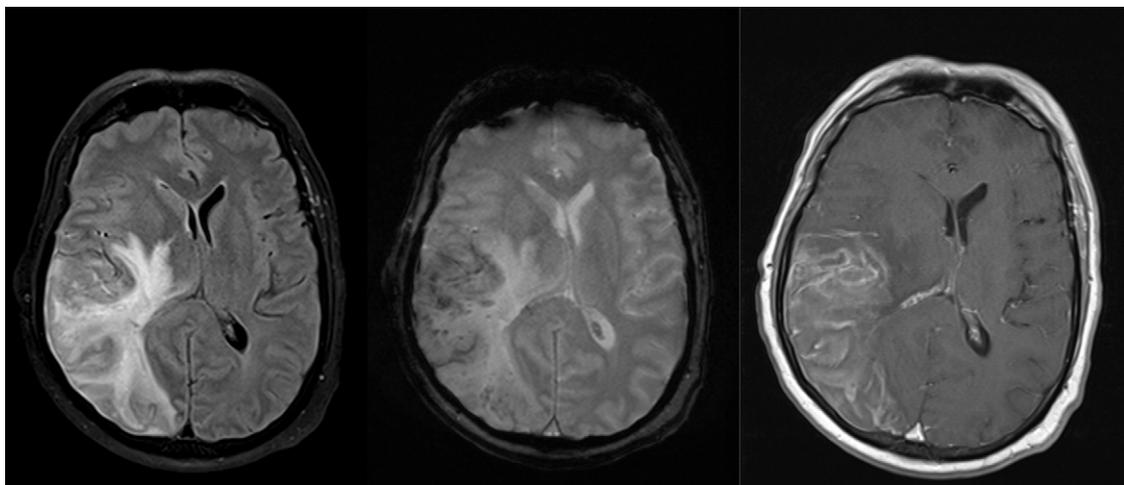


Figure 1 The right-hemispheric lesion area. Brain magnetic resonance images showed extensive vasogenic edema with hemorrhagic foci in the right cerebral hemisphere predominantly in the right perirolandic and fronto-temporal regions with hyperintense signal. Following intravenous gadolinium administration leptomeningeal contrast enhancement in the right temporal lobe was observed.

Table 1 Clinicopathologic features of previously reported cases of H1N1 influenza-associated encephalopathy/encephalitis in adults.

Author	Sex	Age (years)	Interval ILI-neurologic symptoms (days)	Neurologic symptoms	CSF
Fugate et al. ²	Male	40	30	Acute drop on the bispectral index monitor	No pleocytosis Elevated protein level RT-PCR H1N1-ND
Akins et al. ³	Male	20	6	Confusion, seizures	Pleocytosis Elevated protein level RT-PCR H1N1 negative
Chen et al. ⁴	Male	40	2	Tremors, clumsiness, right hemiplegia	Pleocytosis Elevated protein level RT-PCR H1N1-ND
Ito et al. ⁵	Male	26	Unknown	Memory disturbance, disorientation, drowsiness	Mild pleocytosis Normal protein level RT-PCR H1N1 negative
Gonzalez et al. ⁶	Female	46	3	Confusion	No pleocytosis Normal protein level RT-PCR H1N1 negative
Tsai et al. ⁷	Male	46	4	Acute delirium	No pleocytosis Normal protein level RT-PCR H1N1 negative

Author	MRI	EEG	Antiviral therapy	Prognosis
Fugate et al. ²	Subcortical lesions with hemorrhages and edema	Normal	Oseltamivir	Severe sequelae
Akins et al. ³	White matter lesions, diffuse edema	Bilateral diffuse continuous slow δ waves	Oseltamivir 150 mg/dia	Mild sequelae
Chen et al. ⁴	Cortical and subcortical areas of the frontal-parietal lobe	Diffuse slowing of cortical activity	Oseltamivir	Severe sequelae
Ito et al. ⁵	Corpus callosum	Normal	Oseltamivir 150 mg/day	Complete recovery
Gonzalez et al. ⁶	Normal	ND	Oseltamivir	Complete recovery
Tsai et al. ⁷	White matter lesions	Bilateral diffuse continuous slow δ waves	Oseltamivir 150 mg/day	Deceased

ND: not done; ILI: influenza-like illness; CSF: cerebrospinal fluid; EEG: electroencephalography.

airway protection because of a rapid deterioration of his consciousness level. On admission to our hospital, he was found to have right gaze deviation and left-sided hemiplegia. There was no indication for neurosurgical treatment and the patient was admitted to our ICU on suspicion of H1N1-associated encephalitis.

A lumbar puncture was performed. The CSF contained white blood cell count of $<1.0/\mu\text{L}$, no red blood cells, a normal glucose level and an increased protein level. Further work-up to exclude other possible causes of encephalitis included: (1) CSF polymerase chain reaction (PCR) for neurotropic virus was negative, including RT-PCR for 2009 H1N1 virus; (2) Cultures of blood, urine, tracheobronchial aspirate and CSF were negative; (3) Serology for mycoplasma pneumonia, Chlamydia, Rickettsia, hepatitis B and C, syphilis and HIV antibody was negative; (4) Testing for autoimmune disorders was within normal limits.

Brain magnetic resonance images (MRI) revealed extensive vasogenic edema with hemorrhagic foci in the right cerebral hemisphere with hyperintense signal lesions (T2 FLAIR) in left occipital lobe, left cerebellar hemisphere and bulbous. Following intravenous gadolinium administration leptomeningeal contrast enhancement in the right temporal lobe was observed (fig. 1).

After discontinuation of sedation his level of consciousness gradually improved over the following days. Further intensive care course was uneventful and the patient was extubated on day 9. He was discharged on ICU-day 12, conscious, but still with periods of disorientation, and left sided hemiplegia. Almost complete recovery of his hemiplegia was noted one month after ICU discharge.

To the best of our knowledge, this is the first reported case of H1N1-associated encephalitis in an adult patient in Portugal. Although we were not able to identify the H1N1 virus by RT-PCR in the CSF as the causative agent, the combination of clinical and radiological findings and the exclusion of other competing diagnosis are, in our opinion, most consistent with this diagnosis.

H1N1-associated encephalitis was defined by the Center of Disease Control and Prevention as altered mental status >24 h, in patients with laboratory-confirmed H1N1 virus infection, within 5 days of influenza-like illness symptom onset plus two or more of the following: fever, focal neurological signs, CSF pleocytosis, EEG and/or abnormal neuroimaging indicative of encephalitis.¹ Our patient almost fulfilled all of these criteria. However it is noteworthy that neurological signs and symptoms were noted almost 20 days after the initial onset of respiratory illness when sedation was discontinued.

From a review of the English literature, we found one case of acute hemorrhagic leukoencephalitis² and five adult cases of H1N1-associated encephalitis/encephalopathy³⁻⁷ (table 1).

All patients were previously healthy, aged between 20 and 46 years, five were male and one was female. The most frequent initial clinical manifestations were influenza-like symptoms. Neurological symptoms included drowsiness, memory disturbance, disorientation, confusion, tremors and

focal signs starting between 1 and 6 days after onset of illness. All patients had a laboratory-confirmed (nasopharyngeal swab) H1N1 virus infection. However, like in our patient, H1N1 RNA was not detected in CSF by RT-PCR. Other findings of CSF included elevated leukocyte counts and/ or elevated protein levels. Neuroimaging findings were variable ranging from normal to cortical and subcortical lesions, like in our patient, to involvement of deep brain structures with or without brain edema. All patients were treated with Oseltamivir. Two patients received simultaneously treatment with corticosteroids. There was a complete recovery of neurologic manifestations in two patients; in three other patients mild to severe neurologic sequelae were noted.

In conclusion, encephalitis is a rare neurological complication of influenza H1N1 virus in adults. By publishing this case report we hope to contribute by the further characterization of this group of patients. H1N1-associated encephalitis must be considered in the differential diagnosis in patients with influenza-like illness and altered mental status. Diagnosis is based on neurological and neuroimaging findings, and CSF analysis in combination with laboratory-confirmed H1N1 respiratory tract infection.

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